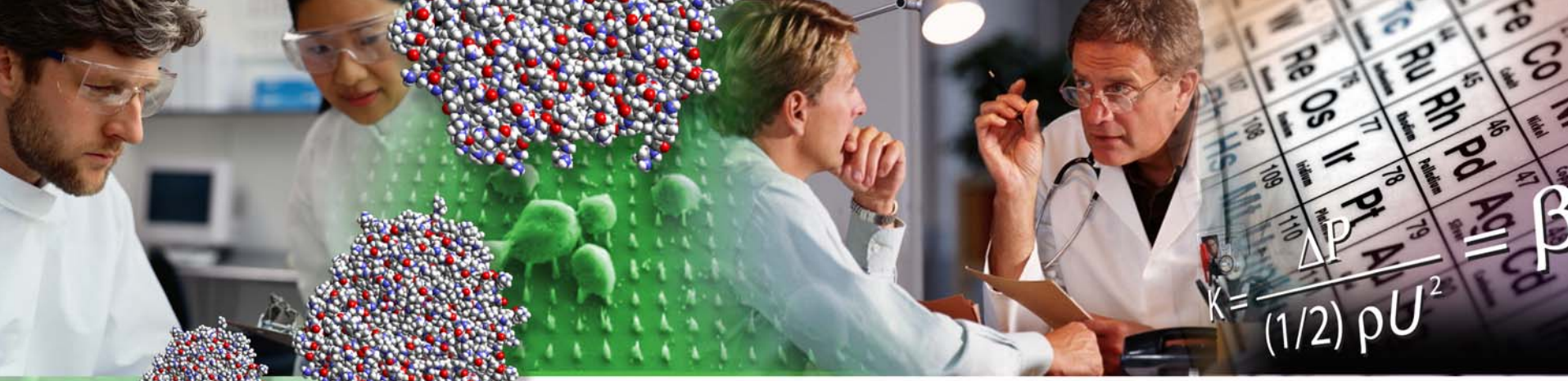


NCI Alliance for Nanotechnology in Cancer

December 14, 2004

PRE-APPLICATION MEETING

Gregory Downing, D.O., Ph.D., *Director*
Office of Technology and Industrial Relations
National Cancer Institute

Today's Agenda

NCI Alliance for Nanotechnology in Cancer

- Programs of the Alliance for Nanotechnology in Cancer
- Funding Process and Timetables
- Expectations for Center and Platform Applications

Alliance Strategies

NCI Alliance for Nanotechnology in Cancer

Major Programs of the Alliance:

1. Centers of Cancer Nanotechnology Excellence
2. Multidisciplinary Research Teams
   - Training
   - Interagency Collaborations
3. Nanotechnology Platforms for Cancer Research
4. Nanotechnology Characterization Laboratory

1 Centers of Cancer Nanotechnology Excellence (CCNEs)

NCI Alliance for Nanotechnology in Cancer

- CCNEs will integrate nanotechnology development into basic and applied cancer research
- Key features of a CCNE:
  - Consortium of ~4 institutions/programs working in a common research area
  - Discrete, specified project performed by named investigators
  - Broad access to array of resources and multidisciplinary expertise
  - 5 – 8 technology platforms
  - Advanced biocomputing capabilities
  - Integration within NCI infrastructure (e.g., Cancer Centers, SPOREs)
  - Affiliation with university or research centers in engineering and physical sciences
  - Partnerships with existing not-for profit/private technology development

1 Centers of Cancer Nanotechnology Excellence(CCNEs)

NCI Alliance for Nanotechnology in Cancer

- 6 key focus areas:
  - Molecular Imaging and Early Detection
  - *In Vivo* Imaging
  - Reporters of Efficacy
  - Multifunctional Therapeutics
  - Prevention and Control
  - Research Enablers
- Funding
  - Specialized centers/cooperative agreement (U54)
  - Funding of 5 centers, $90.8M over 5 years
  - Proposal receipt date: March 25, 2005

2 Multidisciplinary Career Development in Cancer Nanotechnology

NCI Alliance for Nanotechnology in Cancer

- The Alliance will support training and career development initiatives to establish integrated teams of researchers and engineers with backgrounds in cancer biology and nanotechnology
- Funding ($15.5M over 3 years for ~30 awards)
  - F33 National Research Service Awards for Senior Fellows
    - Enables experienced cancer researchers and engineers/physical scientists with directed programs of training to be independent researchers and to provide the future building of training programs
    - Estimate 15 awards of 3 years
  - F32 NRSA Individual Postdoctoral Awards
    - Provides cross-disciplinary research training opportunities for postdoctoral fellows with training in either cancer or technology to gain experience in the other discipline
    - Estimate 15 awards of 3 years
- Proposal receipt date: March 25, 2005

3 Nanotechnology Platforms for Cancer Research

NCI Alliance for Nanotechnology in Cancer

- Individual technology projects to address the 6 key focus areas
- Funding: Research Project Grants (R01)
  - Modeled after Bioengineering Research Partnerships (BRP)/ Bioengineering Research Grants (BRG)
    - Broadly support basic, applied, and translational multidisciplinary research that addresses important biological or medical research problems
    - Partnership must combine bioengineering and/or allied quantitative sciences with biomedical and/or clinical components

4 Nanotechnology Characterization Laboratory (NCL)

NCI Alliance for Nanotechnology in Cancer

- NCL will:
  - Interface with CCNEs, individual investigators, NIST and FDA to develop standards and characterization data for nanoscale devices to help bring these products to market
  - Perform preclinical toxicology, pharmacology, and efficacy testing of nanoscale devices created both by NCI intramural and extramural efforts and by the private sector
  - Facilitate collaborations among the NCI, academia, and the private sector
  - Serve as a nexus for multidisciplinary research, development, and clinical applications
  - Collaborate with other government agencies to leverage resources and expertise

Today's Agenda

NCI Alliance for Nanotechnology in Cancer

- Programs of the Alliance for Nanotechnology in Cancer
- **Funding Process and Timetables**
- Expectations for Center and Platform Applications

Funding Process and Timetable

NCI Alliance for Nanotechnology in Cancer

RFAs published	Nov 30, 2004
Letter of intent	Feb 25, 2004
Proposal receipt date	Mar 25, 2005
Review	July 2004
Council Review	Sept 2005
Funding	Sept 2005

Today's Agenda

NCI Alliance for Nanotechnology in Cancer

- The Programs of the Alliance for Nanotechnology in Cancer
- Funding Process and Timetables
- Expectations for Center and Platform Applications

Who Can Apply?

NCI Alliance for Nanotechnology in Cancer

- Public, private institutions: colleges, universities, hospitals, laboratories
- For-profit or non-profit organizations
- Units of state & local governments
- Eligible agencies of the Federal government
- Domestic institutions and organizations
- Foreign institutions may participate as a subcontractor within a CCNE

Areas of Interest for Nanotechnology Application

NCI Alliance for Nanotechnology in Cancer

- Imaging agents and diagnostics for clinical detection of cancer at presymptomatic stage
- Assessment of therapeutic and surgical efficacy to accelerate clinical translation
- Multifunctional, targeted systems to overcome biological barriers designed to deliver multiple therapeutic agents at local (cell) sites with effective concentrations
- Agents capable of monitoring predictive molecular changes
- Novel approaches to managing symptoms of cancer that compromise quality of life
- Research tools that enable identification of new targets and predict drug resistance

Goals of CCNEs

NCI Alliance for Nanotechnology in Cancer

- Design and test nanomaterials and nanodevices
- Translate their use for clinical research
- Led to novel diagnostic tools and techniques to modulate and overcome cancer processes

Leveraging Existing Infrastructure

NCI Alliance for Nanotechnology in Cancer

- Cancer Centers and SPOREs
- Not exclusive of non-NCI supported resources
- Other NCI sponsored programs that include technology development (not an exclusive list)
  - Early detection research network (validation of detection platforms)
  - Developmental Therapeutics Program
  - Academic Public/Private Partnerships Program (AP4)
  - Integrative Cancer Biology Program
  - Mouse Models of Human Cancer Consortium
  - In vivo Molecular Imaging Centers
  - Development of Clinical Imaging Drug Enhancers

Steering Committee for the Alliance

NCI Alliance for Nanotechnology in Cancer

- An executive management team to provide technical/scientific guidance on program's technology development and management
- Composed of PIs from each CCNE, NCI program manager, CARRA member, and several external advisors
- Conduct quarterly review of milestones, provide technical assessment, facilitate technology and data integration across CCNEs, and provide budgetary recommendations on projects

Principal Investigator

NCI Alliance for Nanotechnology in Cancer

- Demonstrated capabilities, skills, and knowledge in coordinated team (multi-institutional) research with multiple projects and integrated technology development
- Significant level of time and effort
- Breadth of knowledge with nanomaterials and nanoscale assembly
- Experience in platform/product development and commercialization strategies
- Willingness and capability to interact with other CCNE and related nanotechnology program PIs

Principal Investigator

NCI Alliance for Nanotechnology in Cancer

- Demonstrated breadth of knowledge in nanomaterials
- Knowledge/experience of product development, commercialization strategies and/or regulatory requirements
- Not required that PI have primary appointment within cancer center or SPORE
- No Co-PIs
- Demonstrated authority/capability to coordinate and execute decisions on specific projects within CCNE
- Read carefully sections 2.A.1. Principal Investigator Rights and Responsibilities and 2.A.2. NIH Responsibilities

Nanotechnology Platforms to be Considered

NCI Alliance for Nanotechnology in Cancer

- NNI Definition:
  - Research and technology development at the atomic, molecular or macromolecular levels, in the length scale of approximately 1 - 100 nanometer range.
  - Creating and using structures, devices and systems that have novel properties and functions because of their small and/or intermediate size.
  - Ability to control or manipulate on the atomic scale.
- Cancer Nanotechnology Platforms

Cancer Nanotechnology Platforms

NCI Alliance for Nanotechnology in Cancer

- Must propose devices or base materials less than 1000 nM in size although the assembly, synthesis, and/or fabrication of components at dimensions less than 300 nM
- Must incorporate synthetic materials or biomaterials engineered to provide novel properties or modified functions based on nanoscale size
- See examples from nano.cancer.gov
- Encourages development of new platforms aimed at overcoming biological barriers

Cancer Nanotechnology Platforms

NCI Alliance for Nanotechnology in Cancer

- Nanoparticles
  - Variety of compositions: dendrimers, virus-based, carbohydrate-based hydrogels, polymer micelles, Silicon oxide, boronic acid-based, immunoliposomes, peptide nucleic acid conjugates
- Nanoshells
- Nanocantilevers
- Carbon nanotubes

Biological Materials as Nanoplatforms[1]

NCI Alliance for Nanotechnology in Cancer

- Includes bacteriophages/viruses that have unique capabilities to be used as scaffolds for peptide-directed synthesis of magnetic conducting, nanowires, and liquid crystals.
  - Serves as templates for inorganic materials that enables combinatorial synthetic approaches
  - Examples: M13 bacteriophage, tobacco mosaic virus, cowpea mosaic virus
  - Applications: synthesis of nanowires, semiconductors, magnetic materials, films, fluorophores
- NOT to include standard viral gene-therapy vectors (adenovirus, lentivirus etc.) established with recombinant DNA technology

1 Flynn et al. Viruses as vehicles for growth, organization and assembly of materials Acta Materiala 2003;41:5867-5880.

Some Key Issues in Application Preparation

NCI Alliance for Nanotechnology in Cancer

- Pay particular attention to the “musts” – means it should be included or provide rationale why it is not
- Pre-formed group of named investigators that will interact as a multidisciplinary team (do not name external advisors until after review)
- A nanotechnology or nanomaterials synthesis/fabrication component
- An application to cancer research, with an emphasis on translational research
- A focus toward ultimate application in clinical care
- A framework to disseminate research productions, methods and knowledge

Some Key Issues in Application Preparation

NCI Alliance for Nanotechnology in Cancer

- Content and Form of Application Submission (Section 2)
- Part A – Overall Framework
  - Standard facesheet with key program personnel and level off effort
  - Identify 1 or more of the thematic program areas projects will address
  - Abstract page
  - Budget
    - Maximum total budget $5,000,000
    - up to $500,000 in equipment costs in year 1 – requires substantial justification
  - Center specific milestones
  - Limited to 40 pages
- Part B – CCNE Projects
  - 5 – 8 projects (recommend different platforms)
  - Include project specific milestones
  - Team composition should reflect and clearly define skills, knowledge, and experiences to accomplish milestones
  - PI does not need to be on all projects
  - Limited to 25 pages

Some Key Issues in Application Preparation

NCI Alliance for Nanotechnology in Cancer

- Content and Form of Application Submission (Section 2)
- Part C – CCNE Core Support Functions
  - Provides details on key resources/components of the CCNE that will foster interdisciplinary research and technology development – think beyond the projects and investigators to the goals of the Alliance
  - Not expected to be a major portion of the CCNE budget but important functions to be addressed for success of the Alliance
  - Important to show capabilities and examples of:
    - Education, training, and dissemination of research information and tools (i.e. short courses for clinical trialists, seminars fostering collaborative projects using nanotechnology platforms)
    - Technology integration – Means to facilitate bringing new materials, addressing technology problems, building new partnerships (i.e., regional/national programs for technology demonstrations, etc.)
    - Technical evaluation – beta-testing and prototyping
    - Computational programs and theoretical design elements
  - Limited to 50 pages

Nanotechnology Teaming Site

NCI Alliance for Nanotechnology in Cancer

- **Web-based system to facilitate initial communications and exploration of collaborative possibilities**
- **Go to: nano.cancer.gov**
- **Click on “Nanotechnology Teaming Site”**
- **Participants submit basic set of information:**
  - **Position**
  - **Organization**
  - **General areas of expertise possessed**
  - **General areas of expertise sought**
  - **Comments**
- **Participants will then have password access to review other participant information and interests**

NCI-Funded Cancer Nanotech Research to Date

NCI Alliance for Nanotechnology in Cancer

- NCI-Funded Nanotech Programs (39)

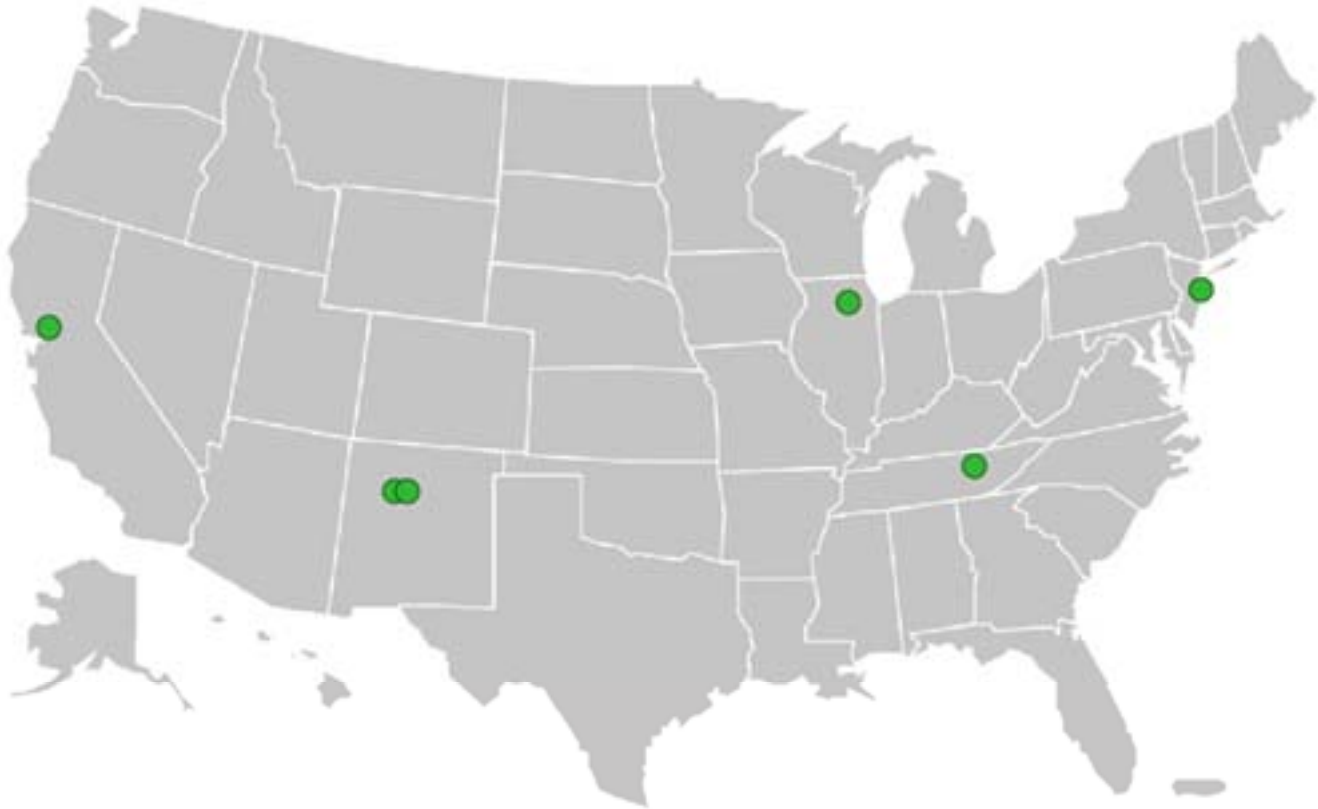
NCI-Funded Cancer Nanotech Research to Date

NCI Alliance for Nanotechnology in Cancer

NCI Cancer Centers (62)

NCI-Funded Cancer Nanotech Research to Date

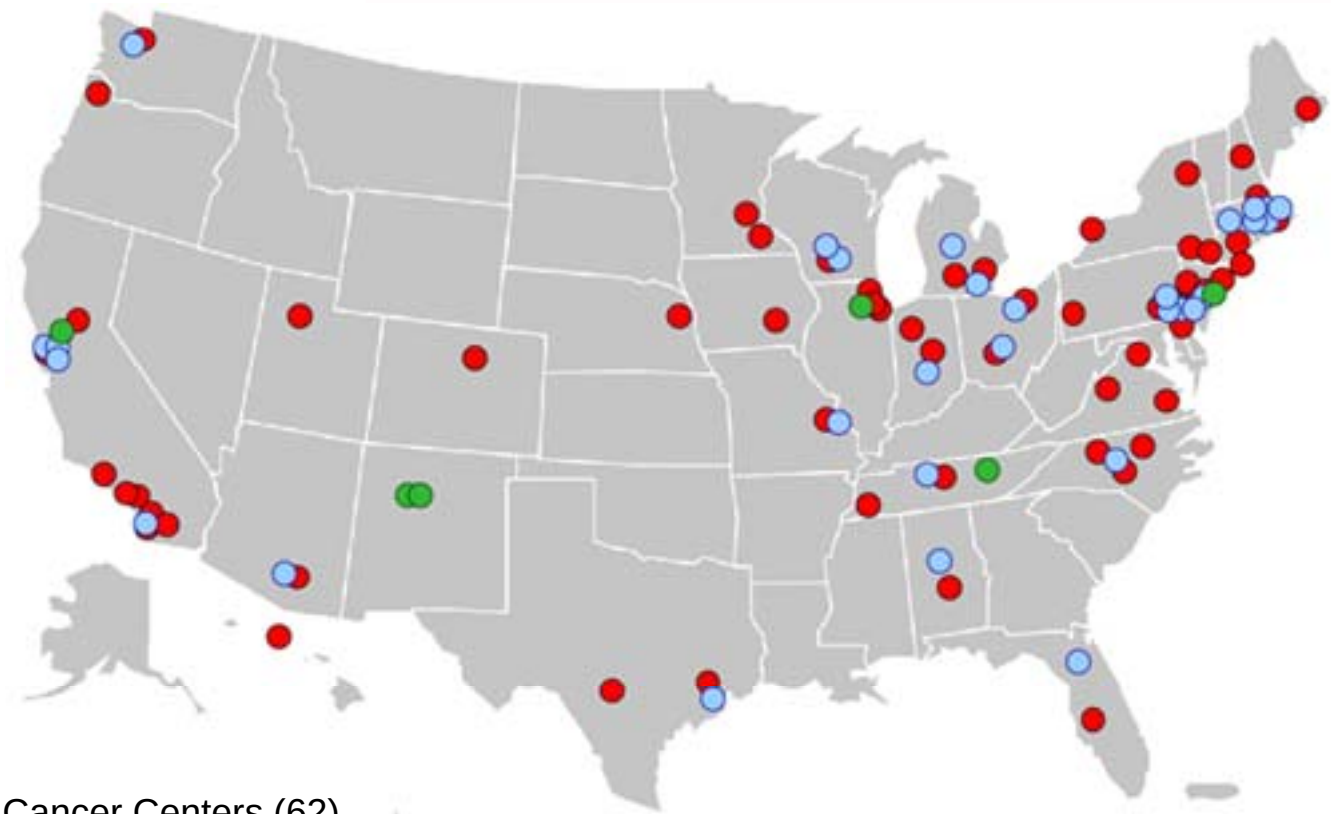
NCI Alliance for Nanotechnology in Cancer



- DOE National Laboratory/Nanoscience Research Centers (NSRCs)(5)

NCI-Funded Cancer Nanotech Research to Date

NCI Alliance for Nanotechnology in Cancer



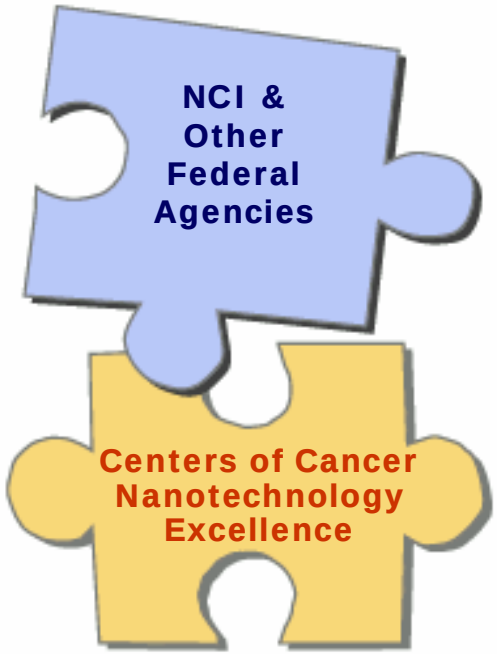
- NCI Cancer Centers (62)
- NCI-Funded Nanotech Programs (39)
- DOE National Laboratory/Nanoscience Research Centers (NSRCs)(5)

Centers of Cancer Nanotechnology Excellence Structure

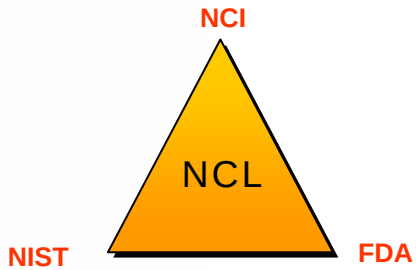
NCI Alliance for Nanotechnology in Cancer

Centers of Cancer Nanotechnology Excellence Structure

NCI Alliance for Nanotechnology in Cancer

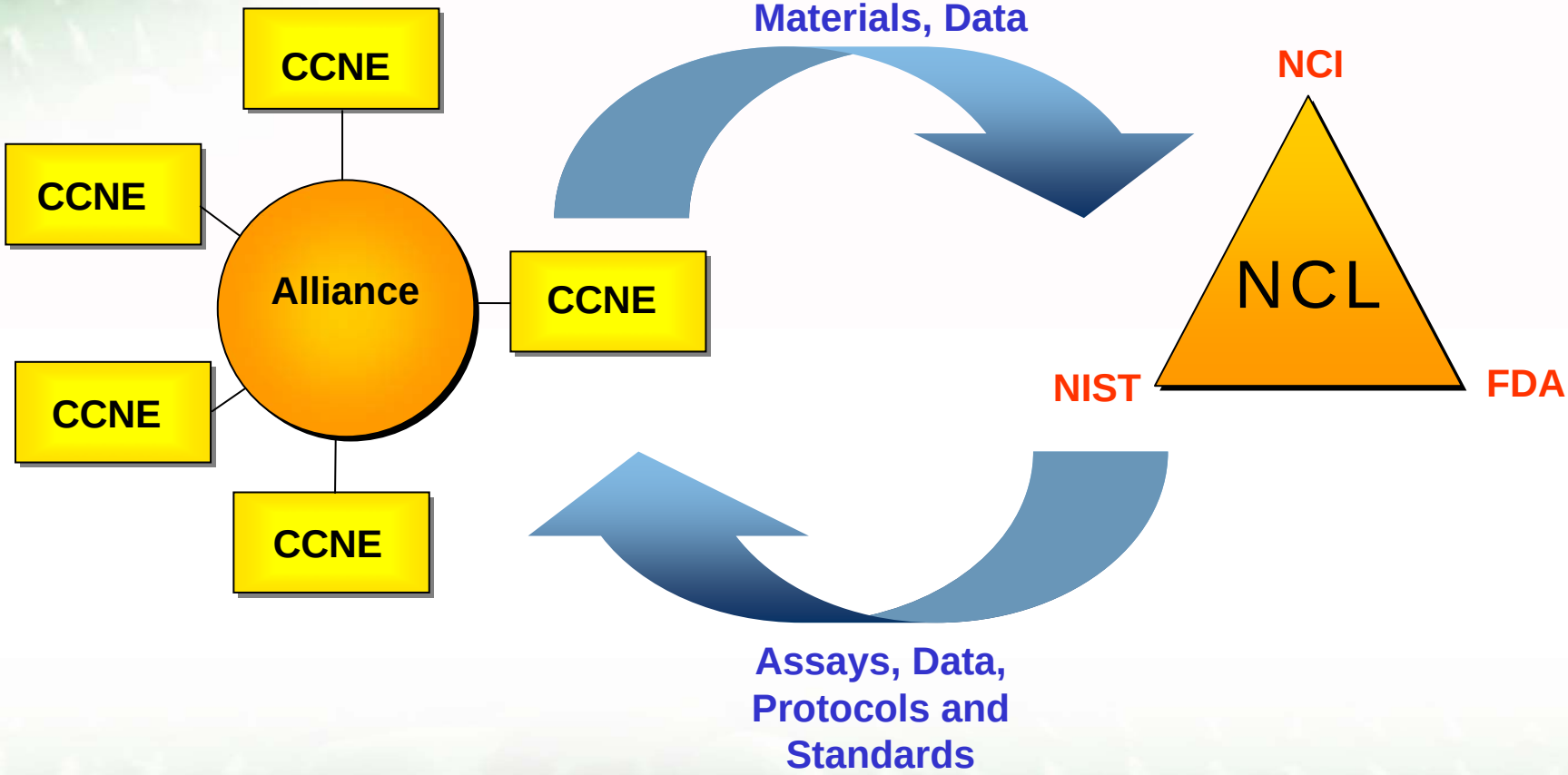


- Administrative Support
- Clinical Trials
- caBIG Data Management
- Communications
- Nanotechnology Characterization Lab



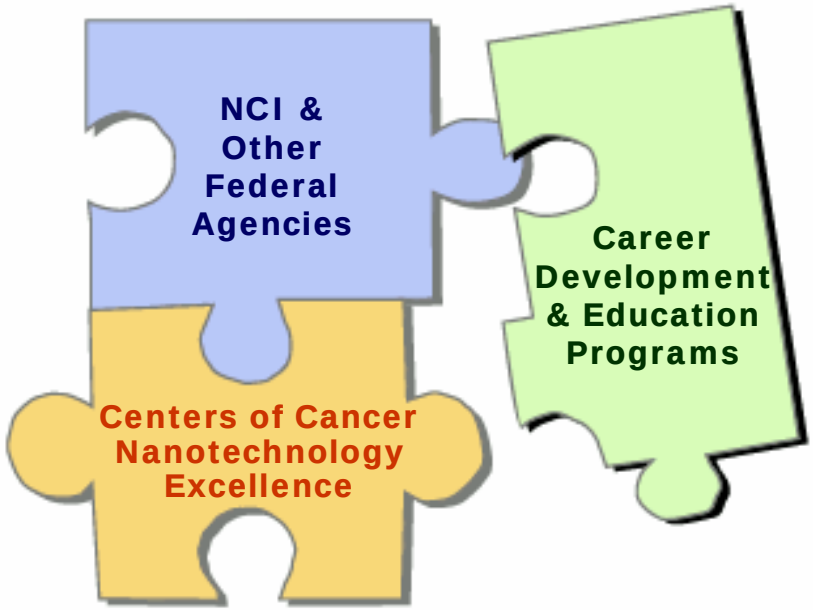
Programmatic Linkage

NCI Alliance for Nanotechnology in Cancer



Centers of Cancer Nanotechnology Excellence Structure

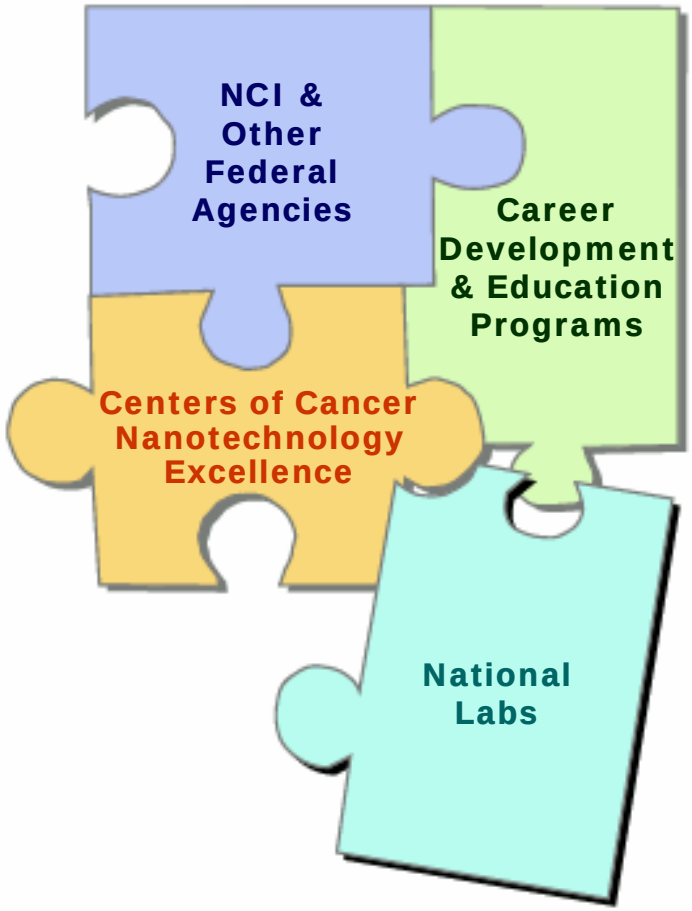
NCI Alliance for Nanotechnology in Cancer



- Multidisciplinary Research Teams
- Fellowships
- Continuing Medical Education
- Undergraduate Education

Centers of Cancer Nanotechnology Excellence Structure

NCI Alliance for Nanotechnology in Cancer

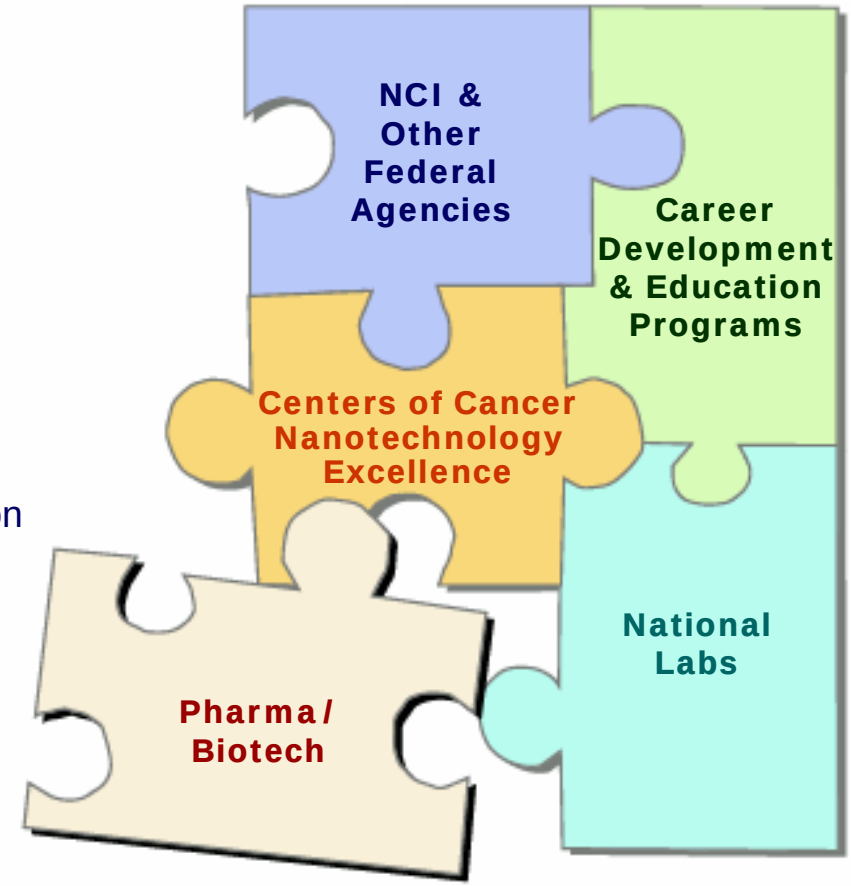


- Multidisciplinary Research Teams
- Materials Fabrication / Synthesis
- Standards
- QA / QC

Centers of Cancer Nanotechnology Excellence Structure

NCI Alliance for Nanotechnology in Cancer

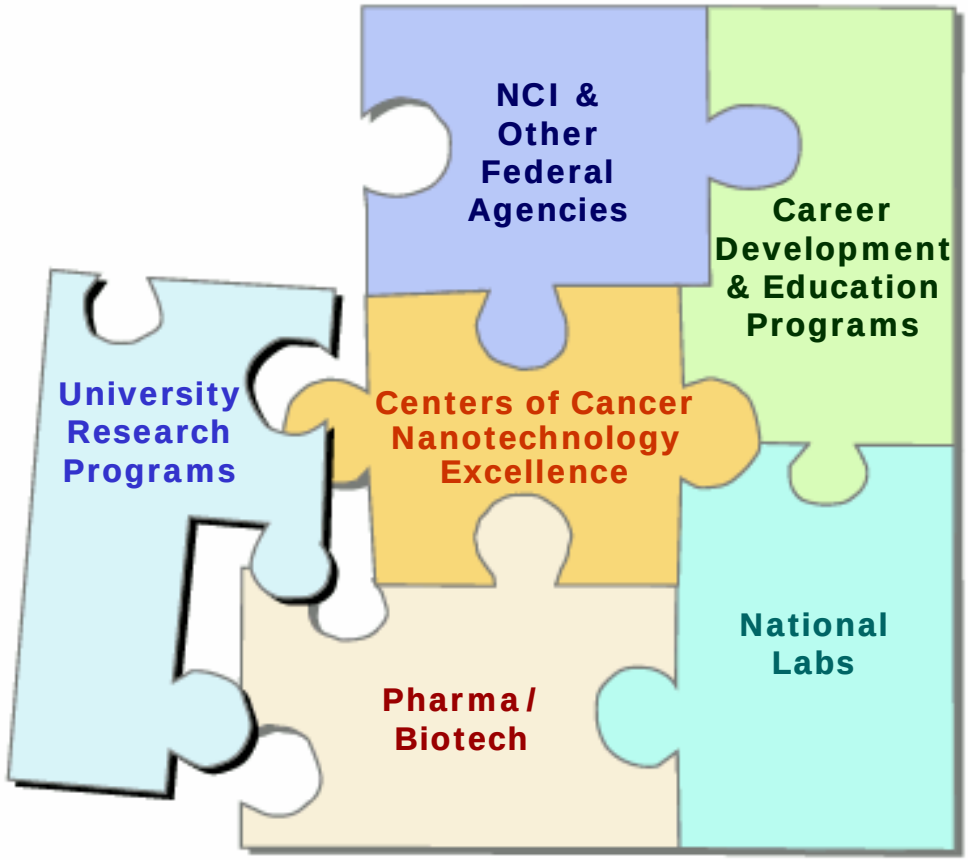
- Partnerships
- Commercialization
- Diagnostic Platforms
- Multivalent Therapeutics



Centers of Cancer Nanotechnology Excellence Structure

NCI Alliance for Nanotechnology in Cancer

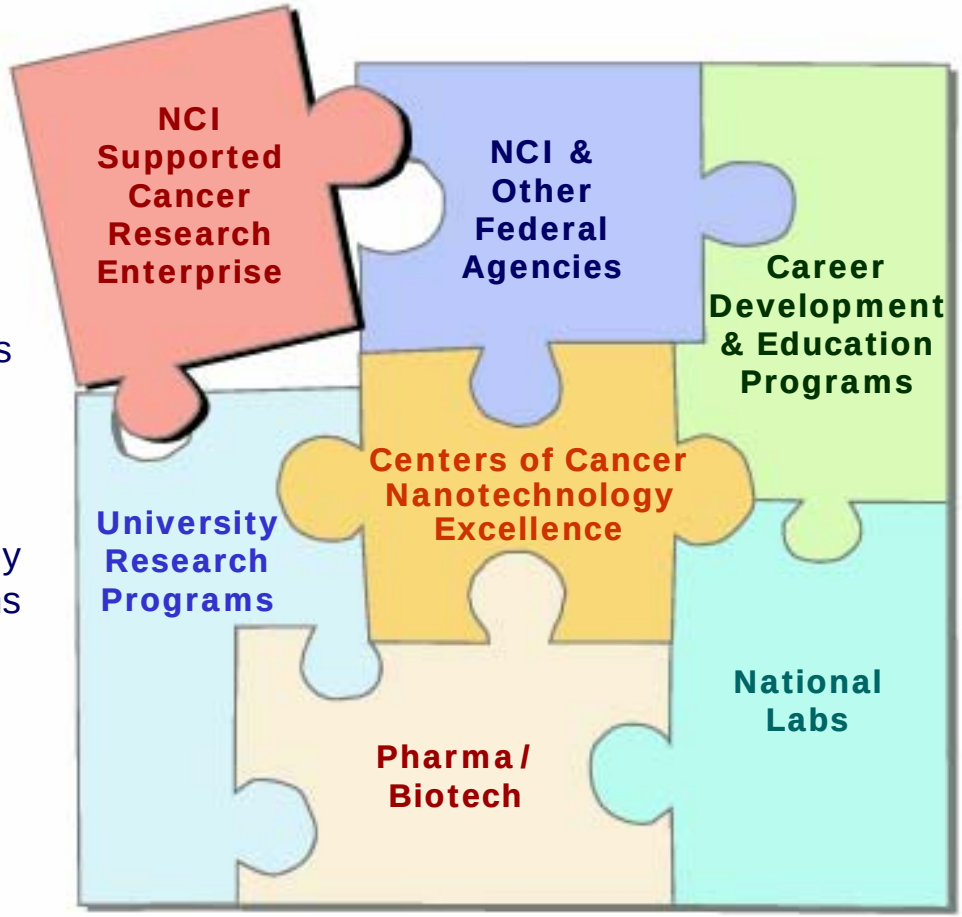
- Integrated Technology Development
- Multidisciplinary Research Teams
- Fundamental Science Programs
- Training / Education



Centers of Cancer Nanotechnology Excellence Structure

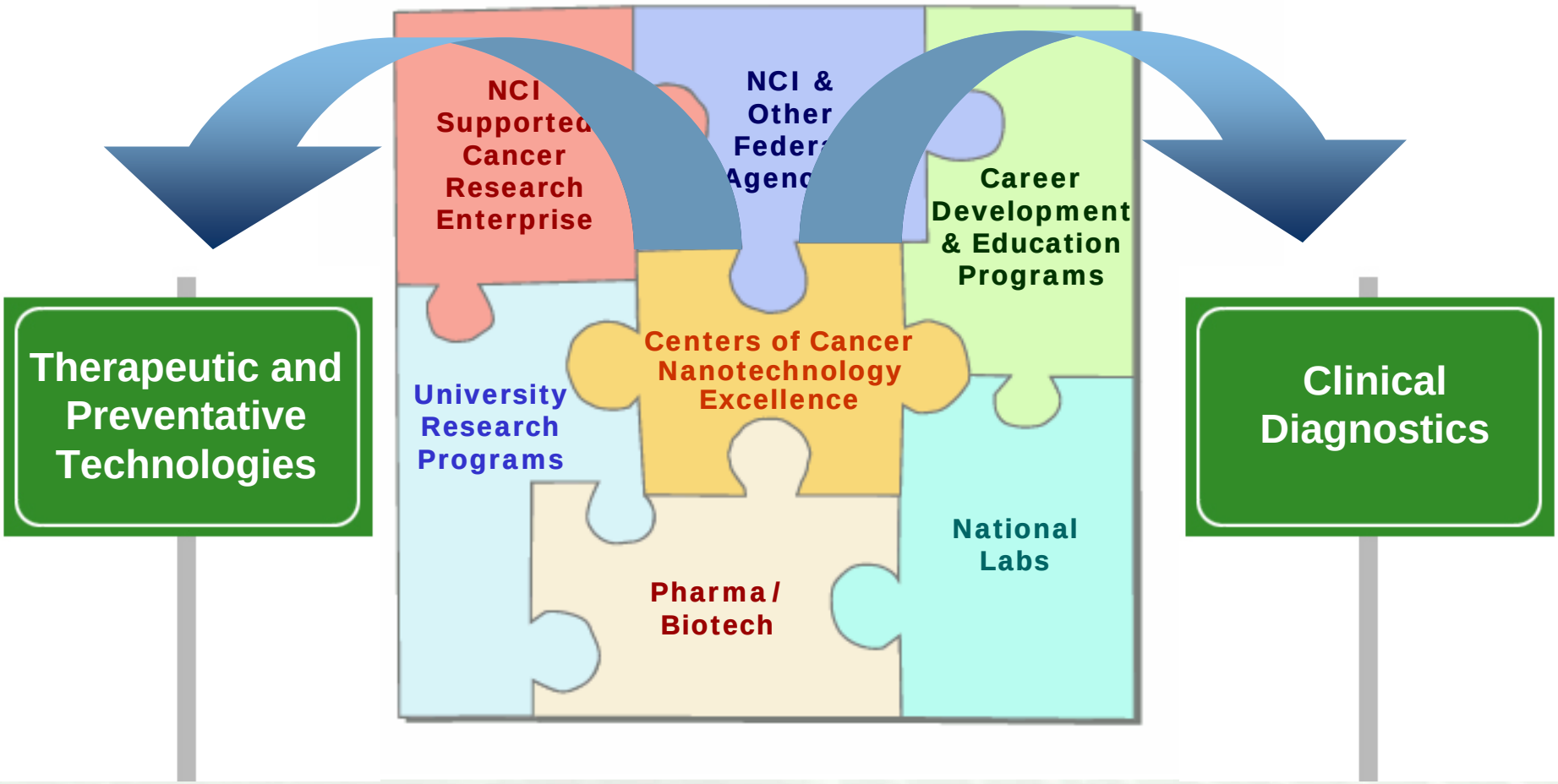
NCI Alliance for Nanotechnology in Cancer

- Cancer Centers, SPOREs, EDRN, Clinical Trials Programs
- Translational Research Support
  - Animal Models
  - Small Animal Imaging
  - DTP, DCIDE
- Integrate Technology from Other Programs
  - IMAT
  - Clinical Diagnostics



Centers of Cancer Nanotechnology Excellence Structure

NCI Alliance for Nanotechnology in Cancer



Nanotech in the Post-genomic Era Promises to Transform Oncology

NCI Alliance for Nanotechnology in Cancer

- Nanoscale cantilevers and nanowire sensors can **detect** biomarkers of cancer from a single cell
- Nanoparticles can aid in **imaging** malignant lesions
- Nanoshells can **kill** tumor cells selectively
- Dendrimers can sequester drugs to **reduce systemic side effects**, deliver multiple drugs to **maximize therapeutic impact**, and **monitor** to discern efficacy rapidly
- Biosensors can monitor genetic changes and hyperplasia to **enable prevention** of cancer progression
- Nanotechnology provides the opportunity for combinatorial therapy, and opens the door to Personalized Medicine

The potential of nanotechnology for cancer research is analogous to the impact of high throughput sequencing on the Human Genome Project

Looking Ahead – Program Performance Measures

NCI Alliance for Nanotechnology in Cancer

Key Opportunity

Molecular imaging and early detection

1 - 3 YEARS	3 - 5 YEARS
▪ Begin clinical trials of nanotechnology-assisted automated assay for rapid detection of genetic abnormalities. ▪ Refine *in vitro* nanotech systems (cantilevers, nanowires, nanochannels) for rapid, sensitive analysis of cancer biomarkers – such systems will be easily expanded as new markers are identified	▪ Disseminate nanoscale devices for routine validation of cancer biomarkers ▪ Develop rapid multi-factorial genomic and proteomic diagnostic system for tumor identification and staging ▪ Begin clinical trails with multi-component nanotechnology platform early diagnosis and therapeutic monitoring

Looking Ahead – Program Performance Measures

NCI Alliance for Nanotechnology in Cancer

Key Opportunity

***In Vivo* Imaging**

1 - 3 YEARS	3 - 5 YEARS
▪ File Investigational New Drug (IND) application to begin clinical trials of nanoscale MRI contrast agents capable of identifying fewer than 100,000 cancer cells. ▪ Conduct clinical trials for three targeted nanoscale imaging agents, using a variety of imaging modalities including MRI, ultrasound, and near infrared optical imaging. ▪ Identify 10 new molecular targets involved in cellular processes for therapeutic development	▪ Complete clinical trials and file New Drug Application (NDA) for first nanoscale imaging agent capable of detecting < 100,000 tumor cells. ▪ Begin clinical trials with multiple nanoscale imaging agents. ▪ Develop capabilities for monitoring active cellular process changes over time.

Looking Ahead – Program Performance Measures

NCI Alliance for Nanotechnology in Cancer

Key Opportunity

Multi-functional Therapeutics

1 - 3 YEARS	3 - 5 YEARS
▪ File IND to begin clinical trials of one targeted sensitizer (radiation, light, magnetic field). ▪ File IND to begin clinical trials of one multifunctional therapeutic complete with accompanying therapeutic assessment tool. ▪ Develop nanoscale devices capable of multivariate targeting and intervention. ▪ File IND to begin clinical trials of one nanoscale therapeutic targeting the reticuloendothelial system.	▪ Conduct multiple clinical trials with targeted sensitizers (radiation, light, magnetic field). ▪ File INDs to begin clinical trials of multiple targeted therapeutics, complete with accompanying therapeutic assessment tool. ▪ File IND to begin clinical trials of one multi-factorial targeted therapeutic agent at IND stage. ▪ Demonstrate five “failed” drugs reconstituted in targeted, “smart” nanoscale devices for retesting in new generation of preclinical models.

Looking Ahead – Program Performance Measures

NCI Alliance for Nanotechnology in Cancer

Key Opportunity

Prevention and Control

1 - 3 YEARS	3 - 5 YEARS
▪ Demonstrate proof of concept for nanoscale device capable of monitoring genetic changes associated with premalignancy or hyperplasia with the aim of preventing subsequent development of cancer.	▪ File IND to begin clinical trials of a nanoscale device capable of identifying markers of premalignancy. ▪ Demonstrate proof of concept for nanoscale device capable of metastasis detection.

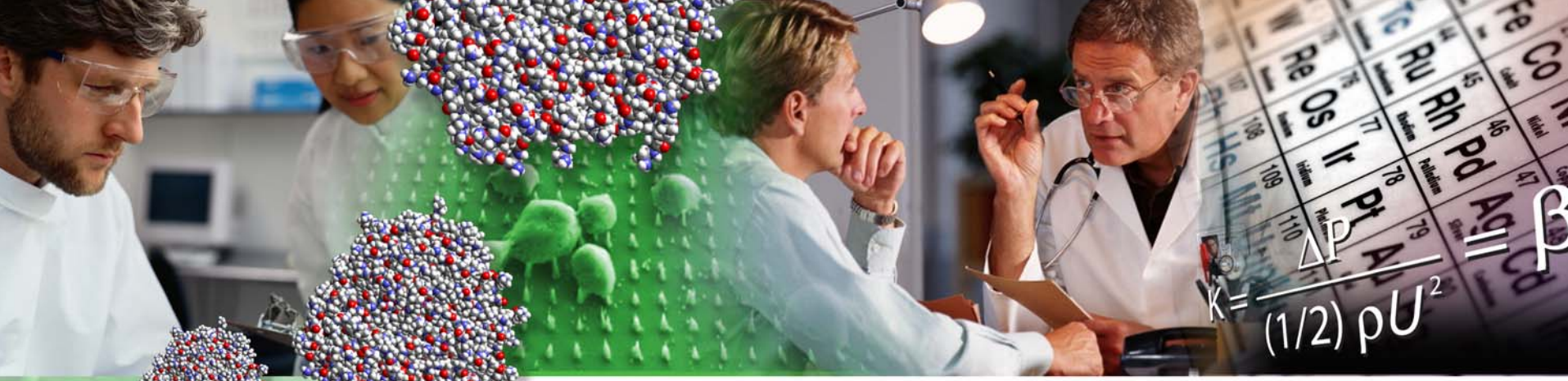
Research Timeline

NCI Alliance for Nanotechnology in Cancer

Key Opportunity

Research Enablers

1 - 3 YEARS	3 - 5 YEARS
▪ Develop nanoscale harvesting devices for proteomics analysis and biomarker identification. ▪ Create prototype for real-time, *in situ* genome sequencing of malignant and pre-malignant cells. ▪ Develop instrumented cell co-culture systems biology research. ▪ Refine cell and cell-component labeling with nanoparticulates such as quantum dots for application to studies of integrated pathways and processes in cancer. ▪ Develop toxicology database for nanoscale devices and nanoparticulates. ▪ Create a scientific framework for regulatory approval of nanoscale diagnostics, therapies, and preventive agents.	▪ Develop nanoscale analytical devices to study DNA methylation and protein phosphorylation. ▪ Promote routine use of nanoscale technology to characterize tumor heterogeneity. ▪ Demonstrate nanoscale technology for detecting multiple mutations *in vivo.* ▪ Promote routine use of nanoscale analytical tools for studying cellular signaling pathways.



NCI Alliance for

Nanotechnology

in Cancer

Website: http://nano.cancer.gov

Email: cancer.nano@mail.nih.gov